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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,287	02/03/2005	Kenji Kogami	SAEG122.002APC	3585
20995	7590	06/20/2008		
KNOBBE MARIENTS OLSON & BEAR LLP			EXAMINER	
2040 MAIN STREET			HAVLIN, ROBERT H	
FOURTEENTH FLOOR			ART UNIT	PAPER NUMBER
IRVINE, CA 92614			1626	
		NOTIFICATION DATE	DELIVERY MODE	
		06/20/2008	ELECTRONIC	

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jcartee@kmob.com  
eOAPilot@kmob.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/523,287	<b>Applicant(s)</b> KOGAMI ET AL.
	<b>Examiner</b> ROBERT HAVLIN	<b>Art Unit</b> 1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 03 April 2008.  
 2a) This action is FINAL.      2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-9 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-9 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 24 August 2007 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/0256/06)  
 Paper No(s)/Mail Date \_\_\_\_\_
- 4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_  
 5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_

### **DETAILED ACTION**

**Status of the Claims:** Claims 1-9 are currently pending.

#### ***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/3/2008 has been entered.

#### ***Declarations***

2. The declaration of Takahashi Naoko under 37 CFR 1.132 filed 4/3/08 is insufficient to overcome the rejection of claims 4 and 5 based upon 35 USC 103 as set forth in the last Office action because: the declaration regarding the search of the prior art is not persuasive as to the nonobviousness of the methyl modification on an amine group. The applicant bears the burden of demonstrating how the result is unexpected from a synthetic chemistry perspective and not a reliance on the absence of a prior art showing of the identical compound. From MPEP 716:

The evidence relied upon should establish "that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance." Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) (Mere conclusions in appellants' brief that the claimed polymer had an unexpectedly increased impact strength "are not entitled to the weight of conclusions accompanying the evidence, either in the specification or in a declaration."); Ex parte C, 27 USPQ2d 1492 (Bd. Pat. App. & Inter. 1992) (Applicant alleged unexpected results with regard to the claimed soybean plant, however there was no basis for judging the practical significance of data with regard to maturity date, flowering date, flower color, or height of the plant.). See also In re Nolan, 553

F.2d 1261, 1267, 193 USPQ 641, 645 (CCPA 1977) and In re Eli Lilly, 902 F.2d 943, 14 USPQ2d 1741 (Fed. Cir. 1990) as discussed in MPEP § 716.02(c)..

Therefore, the declaration was not found persuasive as to the nonobviousness of the claims.

3. The declaration of Satake Syuzo under 37 CFR 1.132 filed 4/3/08 is insufficient to overcome the rejection of claims 4 and 5 based upon 35 USC 103 as set forth in the last Office action because: the declaration that the intermediate compounds are structurally distinct and cannot be used as a material for obtaining the desired product is not persuasive. The fact that the prior art does not teach exactly the same product as instantly claimed is acceptable in a finding of obviousness. This is particularly true when the intermediate is identified in the prior art as a desirable starting material and closely structurally related compounds exist in the art, thereby suggesting to one of ordinary skill in the art to look to these compounds. Therefore, the declaration was not found persuasive as to the nonobviousness of the claims.

#### ***Applicant Arguments***

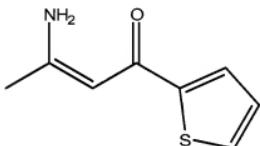
Applicant argues against the obviousness of claims 4 and 5; specifically that the prior art compounds are unrelated to the claimed synthetic pathway. One of ordinary skill in the art is capable of searching the prior art for compounds suggested by Liu et al. as desirable compounds and recognizing structural similarities (such as the methyl positional isomer). In addition, one of ordinary skill in the art would immediately recognize how to modify the reaction to produce the claimed invention. Applicant also argues that the claimed compounds of claims 4 and 5 show unexpected properties because "it is impossible to directly or easily produce the variants of the [claimed

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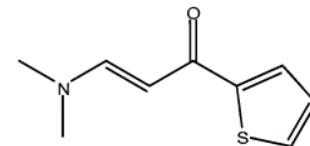
compound]." These arguments are unpersuasive because one of ordinary skill in the art of synthetic chemistry has a very high level of skill and can make inferences based on structural similarities, readily adapt chemical reactions to produce parallel transformations, and is capable of a large amount of experimentation to find the optimal reaction pathways with the best yield and/or purity.

**Prior Claim Rejections - 35 USC § 103**

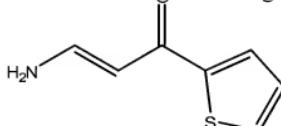
The rejection of claims 4 and 5 under 35 USC § 103(a) is maintained. As discussed above, the declarations filed were not sufficient to overcome this ground of rejection. The prior art teaches, for example the following compounds:



3-amino-1-(2-thienyl)-2-butene-1-one  
Singh et al.

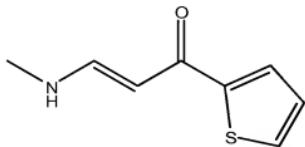


3-dimethylamino-1-(2-thienyl)-2-propen-1-one  
Bogdanowicz-Szwed et al.



3-amino-1-(2-thienyl)-2-propen-1-one  
Cassella Farbwerke et al.

Thus, the prior art suggests the structurally similar instantly claimed compound of:



3-methylamino-1-(2-thienyl)-2-propen-1-one

### NEW Claim Rejections

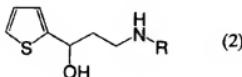
#### *Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

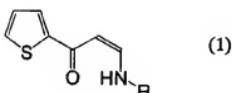
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Chirality, 12:26-29 (2000) in IDS) in view of Makarova et al. (Russian Journal of General Chemistry, Vol. 71, No. 7, 2001, pp. 1126-1129.).

The claims are drawn to a method of making a class of compounds of the formula:

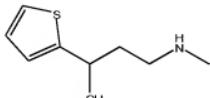


by reducing a compound of the following formula:



Content of the prior art

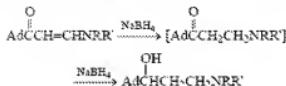
Liu et al. (Chirality, 12:26-29 (2000) in IDS) teaches:



N-methyl-3-hydroxy-3-(2-thienyl)propanamine as "an excellent building block for production of Duloxetine."

Makarova et al. (Russian Journal of General Chemistry, Vol. 71, No. 7, 2001, pp. 1126-1129.) teaches the reduction of beta-aminovinyl ketones to gamma-aminoalcohols in the same manner as in the instant claim. Specifically, on page 1128 Makarova et al. teaches the following general reaction scheme:

the formation of  $\gamma$ -aminoalcohols from  $\beta$ -aminovinyl ketones can be represented by the following scheme.



#### Differences between the prior art and the claims

Liu et al. teaches the identical products as desired in the instant claims. Makarova et al. teaches a method of transforming a structurally similar compound with NaBH4. In Makarova, the only difference is instead of a 2-thienyl group attached to the ketone, there is a cyclic adamantyl group.

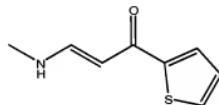
#### Finding of prima facie obviousness

One of ordinary skill in the art would be strongly motivated by the statements in Liu et al. of an "excellent building block for production of Duloxetine." Therefore, one would look to all of the synthetic methods within their technical grasp including reaction

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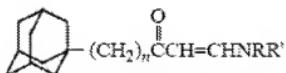
transformations that produce gamma-aminoalcohols (of which the instantly desired product is a member). Finding the successful teachings of Makarova et al. with a structurally similar molecule as the instant claims, one of ordinary skill in the art of synthetic chemistry would immediately recognize the applicability to the teachings of Liu et al. Therefore, one of ordinary skill in the art would look to the teachings of Makarova et al. based on the suggestions of Liu et al. and arrive at the instantly claimed invention. Thus the claims are obvious.

6. Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Chirality, 12:26-29 (2000) in IDS) in view of Makarova et al. (Russian Journal of General Chemistry, Vol. 71, No. 7, 2001, pp. 1126-1129.).

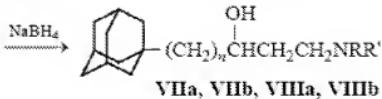


Claims 4 and 5 read on the following compound: 3-methylamino-1-(2-thienyl)-2-propen-1-one.

Makarova et al. also teaches on p 1128:



Va, Vb, VIa, VIb



VIIa, VIIb, VIIIa, VIIIb

V, VII, n = 0, R = H, R' = CH<sub>3</sub> (a); R = H, R' = 1-adamantyl (b). VI, VIII, n = 1, R = H, R' = C<sub>6</sub>H<sub>5</sub> (a); NRR' = piperidyl (b).

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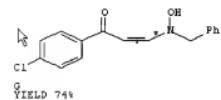
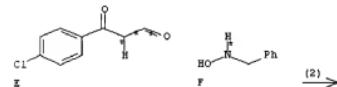
where the amino group is substituted with H and Me. Therefore, the prior art further suggests the specific compound claimed, particularly in light of the desirability of the final product as taught by Liu et al.

7. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Chirality, 12:26-29 (2000) in IDS) in view of Makarova et al., Wright et al. (Journal of Medicinal Chemistry (1992), 35(22), 4061-8) and Guseinov et al. (CASREACT abstract # 122:132250 of Zhurnal Organicheskoi Khimii (1994), 30(4), 496-9).

The claim reads on producing a product of formula (1) from aminating a compound of formula (3) with a monoalkylamine of formula (4).

Wright et al. (Journal of Medicinal Chemistry (1992), 35(22), 4061-8) teaches amination reactions such as those in Table I including:

RX(2) OF 7     ...E + F ==> G



RX(2)     RCT E 51956-73-6, F 522-30-0  
PRO G 141631-05-1  
SOL 57-56-1 MeOH

Guseinov et al. (CASREACT abstract # 122:132250 of Zhurnal Organicheskoi Khimii (1994), 30(4), 496-9) teaches the following amination reactions:



RK-1) PCT I 25246-54-0, II 198-73-9  
PRO C 161045-24-2  
SOL 67-66-3 CHCl<sub>3</sub>



RK-4) PCT I 25246-54-0, II 74-89-5  
PRO J 161045-24-2  
SOL 67-66-3 CHCl<sub>3</sub>

One of ordinary skill in the art would be motivated by the teachings of Liu et al. and Makarova et al. to find a method of synthesizing aminovinyl ketones. One of ordinary skill in the art would be familiar with or be able to look up the known methods of amination. As shown by Guseinov et al. and Wright et al. the same methods of amination are known in the prior art and successfully provide a teaching of the same type of reaction, albeit with somewhat different substitutents, however, one of ordinary skill in the art would immediately recognize the applicability of the reaction method to the teachings of Liu and Makarova. Therefore, the claim is obvious.

8. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (Chirality, 12:26-29 (2000) in IDS) in view of Makarova et al., Wright et al. (Journal of Medicinal Chemistry (1992), 35(22), 4061-8) and Guseinov et al. (CASREACT abstract # 122:132250 of Zhurnal Organicheskoi Khimii (1994), 30(4), 496-9).

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Claim 7 is a combination of the processes of claim 1 and claim 6. As discussed above, claims 1 and 6 are obvious because of the motivation provided by Liu et al., furthermore, the combination of the reaction steps to produce the desired product of Liu et al. is also obvious.

9. Claims 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liu et al. (*Chirality*, 12:26-29 (2000) in IDS) in view of Makarova et al., Wright et al. (*Journal of Medicinal Chemistry* (1992), 35(22), 4061-8) and Guseinov et al. (CASREACT abstract # 122:132250 of *Zhurnal Organicheskoi Khimii* (1994), 30(4), 496-9).

Makarova et al. teaches the use of sodium borohydride in methanol (which is a proton-donating compound). Thus the claims adding specific reactants also taught by the prior art are obvious in light of the obviousness of the parent claims.

#### ***Double Patenting***

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 4, 5 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-2 of copending Application No. 11/989100. Although the conflicting claims are not identical, they are not patentably distinct from each other because E/Z isomers of an alkene are obvious variants. One of ordinary skill in the art would immediately recognize when viewing the double bond of the '100 application that the other isomer would also be desireable.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

#### ***Conclusion***

The claims are not in condition for allowance.

#### ***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT HAVLIN whose telephone number is (571)272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Joe McKane can be reached at (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert Havlin/  
Examiner, Art Unit 1626

/Rebecca L Anderson/  
Primary Examiner, Art Unit 1626